limited the development of specific treatment whereas the gold standard treatment is little tolerated. In the context of cardiomyocytes death or life, this study purposes to investigate the role of endoplasmic reticulum (ER) stress and hypoxia inducible factor-1 (HIF-1) in myocardial susceptibility to ischemia-reperfusion (I/R) induced by chronic IH.

Methods: C57Bl6J, HIF-1$\alpha^{+/-}$ and their control mice were exposed to 14 days of IH (21–5% FiO2, 60s cycle, 8h/day). Then, mice were submitted to an in vivo ischemia-reperfusion to assess infarct size (IS, in % relative to area at risk) or hearts were removed to assess ER stress markers and HIF-1 activity using Western-blot and ELISA. In additional groups, TUDCA (an ER stress inhibitor, 75mg. kg^{-1}) was administered daily during N or IH exposition to assess the role of ER stress in IH-susceptibility to I/R.

Results: Whereas chronic IH induced an increase in infarct size (33.7±9.4 *vs* 61.0±5.6% in N and IH groups, respectively, p<0.05), IH failed to increase infarct size in HIF1$\alpha^{+/-}$ mice (42.4±2.7 *vs* 24.7±3.4 % in HIF1$\alpha^{+/-}$-N and HIF1$\alpha^{+/-}$-IH, respectively). An increase in HIF-1 activity and ER stress markers was also observed in IH-mice. By the way, TUDCA totally abolished the IH-increased in infarct size (49.9±3.0 *vs* 61.0±5.6% in IH-TUDCA, respectively) as well as the IH-increased in HIF-1 activity (1.3±0.04 *vs* 0.14±0.02 fold increase in IH and IH/TUDCA, p<0.0001 *vs* non treated mice).

Conclusion: These results suggest that the "ER stress-HIF-1"axe should be considered in apneic patients as a potential therapeutic target to limit myocardial ischemic damages.

0093

Therapeutic hypothermia induced by total liquid ventilation reduces cardiac and cerebral production of free radicals after non shockable cardiac arrest

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Introduction: Ultra-fast cooling induced by total liquid ventilation (TLV) has been shown to be potently neuro and cardioprotective after shockable cardiac arrest and/or acute myocardial infarction**.** In this study we examined a possible underlying mechanism of this protection, in particular reduced free radicals production.

Methods and Results: Thirty six rabbits subjected to asphyxia cardiac arrest were divided into three groups: normothermic life support (Control group, n=12) or hypothermia induced by either i.v. cold saline (CONV group; n=12) or by TLV (TLV group, n=12). Using electronic paramagnetic resonance spectroscopy (EPR) and 1-hydroxy-3-methoxycarbonyl-2,2,5,5-tetramethylpyrrolidine hydrochloride (CMH) as spin probe, we observed a decrease in the production of free radicals in various organs including the heart and the cerebral cortex in TLV and CONV groups as compared to Control, however the effect of TLV was significantly more marked. These results were associated with a significant improvement of the neurological status and an increase in the survival rate as compared to Control and CONV groups.

Conclusion: Therapeutic hypothermia induced by TLV could be a promising approach to improve organ preservation before irreversible alteration by free radicals.

0309

Cardioprotective effect of a novel snake venom derived natriuretic peptide during myocardial ischemia reperfusion injury

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Introduction: In this study, we aimed at testing the therapeutic potential of a novel Natriuretic Peptide (NPs), identified from Tunisian snake venom, when administered during reperfusion.

Materials and Methods: Langendorff perfused male Wistar rat hearts were subjected to 30min regional coronary artery occlusion followed by 90min reperfusion. Hearts were treated either with brain natriuretic peptide BNP (10nM) or NPs (200nM). In another set of experiments, hearts were pretreated with either isatin (100µM), a natriuretic peptide receptors blocker or 5HD (10µM), a mitochondrial KATP channels blocker. Post ischemic cardiac haemodynamic parameters, using Labt Chart (ADInstruments) and infarct size (IS), using planimetry, were evaluated. Western blotting experiments for studying cGMP and Reperfusion Injury Salvage Kinases pathways were performed. Calcium Retention Capacity (CRC) to evaluate the mitochondrial function was also assessed by oxygraphy.

Results: BNP and NPs significantly decreased the IS by 60% and 62% respectively compared to control non treated hearts (p<0.001). Regarding hemodynamic parameters, both BNP and NPs improved the developed pressure (DP) by 135 % and 152 % respectively (p<0.05). These beneficial effects are abolished after pretreatment by isatin or 5HD. NPs significantly increased the expression of pAKT, pGSK3ß and PKCε when BNP increased pERK1/2 compared to control group. Both BNP and NPs increased the CRC by 124% and 86% respectively compared to control group.

Conclusion: Our results demonstrate that NPs and BNP have cardioprotective effects during acute myocardial ischemia. These effects are mediated, for both drugs, by natriuretic receptors and by the activation of mitochondrial KATP channels. The cardioprotection involves the two PI3K/Akt/ERK and cGMP-PKC signaling pathways which converge to the mitochondria. Administration of NPs may provide a novel therapeutic strategy in acute myocardial isch

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